

PATENT  
Customer No. 22,852  
Attorney Docket No. 3806.0050-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: )  
BLANCHE et al. ) Group Art Unit: 1652  
Application No.: 10/724,598 ) Examiner: K. Kerr (Prior Appln.)  
Filed: December 1, 2003 ) Confirmation No.: 8180  
)  
For: METHODS OF INCREASING THE PRODUCTION  
OF COBALAMINS USING COB GENE EXPRESSION (As Amended)

MAIL STOP AMENDMENT  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

REQUEST FOR CORRECTED FILING RECEIPT

We are forwarding a copy of a Filing Receipt for this application. The information under Domestic Priority data as claimed by applicant contained a typographical error. Therefore, under Domestic Priority data as claimed by applicant, please delete "which is a CON of 07/916,451 07/17/1992 ABN" and insert the following:

-- which is a CON of 07/916,151 09/14/1992 ABN  
which is a national stage of PCT/FR91/00054 01/30/1991 ABN --

Application No. 08/426,630, which is a continuation of Appln. No. 07/916,151, issued as U.S. Patent No. 6,656,709 B1. The attached copy of the face page of the '709 patent correctly identifies that it is a continuation of Appln. No. 07/916,151. The '709 patent also correctly indicates that 07/916,151 was filed as PCT/FR91/00054, and

is therefore a national stage application. The 35 U.S.C. § 371 date of Appln. No. 07/916,151 is September 14, 1992.

It is respectfully requested that a corrected Filing Receipt be issued as soon as possible.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Dated: November 8, 2004

By:   
\_\_\_\_\_  
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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY.DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/724,598	12/01/2003	1652	0.00	03806-0050-02000	189	57	4

22852

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER  
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RECEIVED

FILING RECEIPT



\*OC000000013487162\*

AUG 11 2004

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, LLP

Date Mailed: 08/09/2004

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s)

Francis Blanche, Paris, FRANCE;  
Beatrice Cameron, Paris, FRANCE;  
Joel Crouzet, Paris, FRANCE;  
Laurent Debussche, Paris, FRANCE;  
Sophie Levy Schil, Paris, FRANCE;  
Denis Thibaut, Paris, FRANCE;

Assignment For Published Patent Application

Aventis Pharma S.A.;

Domestic Priority data as claimed by applicant

This application is a CON of 08/426,630 04/21/1995 PAT 6,656,709  
which is a CON of 07/916,451 07/17/1992 ABN

(\*)Data provided by applicant is not consistent with PTO records.

Foreign Applications

FRANCE 90 01137 01/31/1990

--which is a CON of 07/916,151 09/14/1992 ABN  
which is a national stage of  
PCT / FR 91 / 00054 01/30/91 ABN

If Required, Foreign Filing License Granted: 08/09/2004

Projected Publication Date: To Be Determined - pending completion of Missing Parts

Non-Publication Request: No

RTK

AUG 12 2004

7/11/04  
9/16/04  
RTK

**Early Publication Request: No**

**Title**

Methods of increasing the production of cobalamins using cob gene expression

**Preliminary Class**

435

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**LICENSE FOR FOREIGN FILING UNDER  
Title 35, United States Code, Section 184  
Title 37, Code of Federal Regulations, 5.11 & 5.15**

**GRANTED**

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

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**NOT GRANTED**

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).



(12) **United States Patent**  
Blanche et al.

(10) Patent No.: **US 6,656,709 B1**  
(45) Date of Patent: **Dec. 2, 2003**

(54) **METHODS OF INCREASING THE PRODUCTION OF COBALAMINS USING COB GENE EXPRESSION**

(75) Inventors: **Francis Blanche, Paris (FR); Beatrice Cameron, Paris (FR); Joel Crouzet, Paris (FR); Laurent Debussche, Paris (FR); Sophie Levy Schill, Paris (FR); Denis Thibaut, Paris (FR)**

(73) Assignee: **Rhone-Poulenc Biochimie, et al., Antony (FR)**

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/426,630**

(22) Filed: **Apr. 21, 1995**

**Related U.S. Application Data**

(63) Continuation of application No. 07/916,151, filed as application No. PCT/FR91/00054 on Jan. 30, 1991, now abandoned.

(30) **Foreign Application Priority Data**

Jan. 31, 1990 (FR) ..... 90 01137

(51) **Int. Cl. 7** ..... C12P 19/42

(52) **U.S. Cl.** ..... 435/86

(58) **Field of Search** ..... 536/232, 23.7; 435/320.1, 240.2, 252.3, 69.1, 86, 232

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

3,018,225 A \* 1/1962 Long ..... 435/86

**FOREIGN PATENT DOCUMENTS**

WO WO A 8701391 12/1987

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Brey et al., J. Bacteriol. 167: 623-630 (1986).<sup>\*</sup>

Crouzet et al., J. Bacteriol. 172: 5968-5979 (Oct. 1990).<sup>\*</sup>

Crouzet et al., J. Bacteriol. 172: 5980-5990 (Oct. 1990).<sup>\*</sup>

Cameron et al., J. Bacteriol. 173: 6058-6065 (1991).<sup>\*</sup>

Cameron et al., J. Bacteriol. 173: 6066-6073 (1991).<sup>\*</sup>

Crouzet et al., J. Bacteriol. 173: 6074-6087 (1991).<sup>\*</sup>

Cameron, et al.; "Cloning and analysis of genes involved in coenzyme B12 biosynthesis in *Pseudomonas denitrificans*", pps. 547-557; *Journal of Bacteriology*, vol. 171, No. 1, Jan. 1989; American Society for Microbiology (Washington, D.C. US).

Blanche, et al.; "Purification and characterization of S-adenosyl-L-methionine: Uroporphyrinogen III methyl-transferase from *Pseudomonas denitrificans*", pps. 4222-4231; *Journal of Bacteriology*, vol. 171, No. 8, Aug. 1989; American Society for Microbiology, (Wash. D.C. ).

\* cited by examiner

**Primary Examiner**—Ponnathapu Achutamurthy

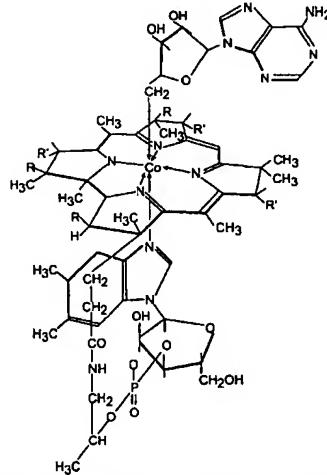
**Assistant Examiner**—Kathleen Kerr

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(57) **ABSTRACT**

Novel polypeptides involved in the biosynthesis of cobalamines and/or cobamides, in particular coenzyme B<sub>12</sub>, genetic material responsible for expressing these polypeptides, and a method for preparing them, are described. A method for amplifying the production of cobalamines, and particularly coenzyme B<sub>12</sub>, using recombinant DNA techniques, are also described.

**58 Claims, 189 Drawing Sheets**



ADENOSYLCOBALAMIN R = CH<sub>2</sub>COHN<sub>2</sub>, R' = CH<sub>2</sub>CH<sub>2</sub>CONH<sub>2</sub>



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APPLICATION NUMBER	FILING OR 371 (c) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO/TITLE
10/724,598	12/01/2003	Francis Blanche	03806-0050-02000

**CONFIRMATION NO. 8180**

22852  
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\*OC000000013489504\*

Date Mailed: 08/09/2004

## Notice Regarding Benefit/Priority Claim(s)

### **Improper Benefit Claim(s) to Prior-Filed Nonprovisional Application(s)**

The benefit claim(s) to prior-filed nonprovisional application(s) is improper because there is no specific reference for each prior-filed application that includes: (1) the identification of the prior-filed application by application number, or international application number and international filing date; and (2) a clear indication the relationship (i.e., continuation, divisional, or continuation-in-part) of the nonprovisional applications. For example, applicant should amend the specification to include a specific reference, such as "This application is a continuation of Application No. 10/---,--- filed ---." in the first sentence of the specification following the title.

Applicant should review each benefit claim submitted and, if appropriate, provide the proper reference to the prior-filed application(s) as required by 37 CFR 1.78. A proper relationship includes an identification of each nonprovisional application as a continuation, divisional or continuation-in-part application of the immediate prior-filed nonprovisional application for which a benefit is claimed under 37 CFR 1.78 in order to establish copendency throughout the entire chain of prior-filed applications. The specific reference must be included in the domestic priority information section of an application data sheet (37 CFR 1.76), or the specification must contain, or be amended to contain, such reference in the first sentence following the title.

**Timeliness:** The required reference for each benefit claim must be filed during the pendency of the instant application and within the later of: (1) four months from the actual filing date of the instant application, or the national stage commencement date if the instant application is a national stage application under 35 U.S.C. 371; or (2) sixteen months from the filing date of the prior-filed application. Failure to timely file the required reference is considered a waiver of any benefit claim, unless a grantable petition to accept an unintentionally delayed claim under 37 CFR 1.78(a), the surcharge set forth in 37 CFR 1.17(t), and the required reference are filed. See 37 CFR 1.78(a).

### **Improper Benefit Claim(s) to Prior-Filed Nonprovisional Application(s)**

The benefit claim(s) to prior-filed provisional application(s) is improper because the instant application was not filed within twelve (12) months from the filing date of the provisional application,

and there is no indication of an intermediate nonprovisional application that is directly claiming the benefit of the provisional application and filed within 12 months of the filing date of the provisional application. For example, applicant should amend the specification to include a specific reference, such as "This application is a continuation of Application No. 10/---,--- filed ---, which claims the benefit of U.S. Provisional Application No. 60/---,--- filed---." in the first sentence of the specification following the title.

Applicant should review each benefit claim submitted and, if appropriate, provide the proper reference to the prior-filed applications (including an indication of any intermediate nonprovisional application that is directly claiming the benefit of the provisional application and filed within 12 months of the filing date of the provisional application) as required by 37 CFR 1.78. The required reference must be included in the domestic priority information section of an application data sheet (37 CFR 1.76), or the specification must contain, or be amended to contain, such reference in the first sentence following the title.

**Timeliness:** The required reference for each benefit claim must be filed during the pendency of the instant application and within the later of: (1) four months from the actual filing date of the instant application, or the national stage commencement date if the instant application is a national stage application under 35 U.S.C. 371; or (2) sixteen months from the filing date of the prior-filed application. Failure to timely file the required reference is considered a waiver of any benefit claim, unless a grantable petition to accept an unintentionally delayed claim under 37 CFR 1.78(a), the surcharge set forth in 37 CFR 1.17(t), and the required reference are filed during the pendency of the instant application.

#### **Improper Priority Claim(s) to Prior-Filed Foreign Application(s)**

The instant application was not filed within twelve (12) months from the filing date of the prior-filed foreign application, and there is no benefit claim to an intermediate nonprovisional application filed within 12 months of the filing date of the foreign application. Applicant should review each priority claim submitted and, if appropriate, provide the proper reference to any intermediate nonprovisional application filed within 12 months of the filing date of the foreign application in compliance with 37 CFR 1.78, or delete the priority claim. The required reference to an intermediate nonprovisional application must be included in the domestic priority information section of an application data sheet (37 CFR 1.76), or the specification must contain, or be amended to contain, such reference in the first sentence following the title.

**Timeliness:** The required reference for the benefit claim to an intermediate nonprovisional application must be filed during the pendency of the instant application and within the later of: (1) four months from the actual filing date of the instant application, or the national stage commencement date if the instant application is a national stage application under 35 U.S.C. 371; or (2) sixteen months from the filing date of the prior-filed application. Failure to timely file the required reference is considered a waiver of any benefit claim, unless a grantable petition to accept an unintentionally delayed claim under 37 CFR 1.78(a), the surcharge set forth in 37 CFR 1.17(t), and the required reference are filed.

#### **Benefit Claims to More Than 400 Prior-Filed Applications**

The Office's automated system to record and capture benefit claims is only capable of recording benefit claims for 400 prior-filed applications. Therefore, the Office is unable to generate a filing receipt containing benefit claims for more than 400 prior-filed applications even though applicant is entitled to submit benefit claims for more than 400 prior-filed applications. Accordingly, applicant should not request a corrected filing receipt to include benefit claims for more than 400 prior-filed applications.

**Prior-Filed Nonprovisional Application has been Improperly Indicated as a National Stage (35**

### **U.S.C. 371) Application**

Applicant submitted a benefit claim to a prior-filed nonprovisional application and improperly indicated that the prior-filed application is a national stage application under 35 U.S.C. 371. The Office's records show that the prior-filed application is an application filed under 35 U.S.C. 111(a). The Office has entered the benefit claim to the prior-filed application as a benefit claim to an application filed under 35 U.S.C. 111(a). Any request for a corrected filing receipt to include the indication that the prior-filed application is a national stage application will not be granted unless applicant supplies evidence that the prior application was in fact a national stage application. Accordingly, applicant should not submit such request without such evidence. Applicant should submit an amendment (or an application data sheet (ADS) if the benefit claim was submitted in an ADS) to delete the indication that the prior-filed application is a national stage application.

For more information and examples on benefit claims, please see Claiming the Benefit of a Prior-Filed Application under 35 U.S.C. 119(e), 120, 121, and 365(c), 1268 Off. Gaz. Pat. Office 89 (March 18, 2003), which is available on the USPTO website at <http://www.uspto.gov/web/offices/com/sol/og/2003/week11/patbene.htm>, and the Manual of Patent Examining Procedure (MPEP) §§ 201.11 and 201.14.

### **PART 2 - COPY TO BE RETURNED WITH RESPONSE**